

August 2, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Manuscript 130802.docx).

Title: To Determine the Relationship Between Time of Infliximab Therapy Initiation and Infliximab Dose Escalation - A Retrospective Study

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Name of Journal: World Journal of Gastroenterology

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We very much appreciate the opportunity to resubmit our manuscript. We feel with the reviewers thoughtful suggestions our manuscript has improved. This work provides further insight to clinicians in optimizing anti TNF therapy for patients with Crohn's disease

The manuscript has been improved according to the suggestions of reviewers:

1. Format has been updated

2. Revision has been made according to the suggestions of the reviewer

(1) This is a retrospective study; therefore data on mucosal healing is not available. Infliximab trough levels, anti-TNF immunoglobulins, fecal calprotectin were not available at the time of this study period. Smoking and concurrent prednisone use were collected but were not significant in the univariate analysis, so were not included in the multivariate analysis (this information is now added to Table 1).

(2) The term "immunosuppressives" were changed to "immunosuppressants" and definition provided. The reviewer may have mis-read the sentence regarding the role of TNFa and pathogenicity of Crohn's disease. The sentence is describing TNFa, the cytokine, and it's role in the pathogenesis of Crohn's disease, and not anti-TNF agents. The 7 patients excluded as they had been exposed to biologics in the past (and not based on Harvey-Bradshaw Index). Table 2 is a univariate and multivariate analysis to find out which clinical variables has most impact on dose escalation. Once it was determined that "years between diagnosis and therapy initiation" and "concurrent

immunosuppressant therapy” has the most impact, these groups were analysed separately with the Fisher’s exact test. This is a retrospective study and the 4 groups identified for analysis were determined through a multivariate analysis, and dose escalation is the factor being assessed; therefore, only 4 groups were included (not 8).

3. References and typesetting were corrected

Thank you again for publishing our manuscript in the World Journal of Gastroenterology.

Sincerely,

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